REMARKS

Reconsideration of this application is respectfully requested.

Claims 2-24 and 245-251 were previously pending in this application. Claims 2-24 have been canceled. Claims 246, 247 and 251 have been amended above. No claims have been added. Accordingly, claims 245-251 as amended are presented for further examination.

The first page (line 1) of the specification has been amended by inserting information cross-referencing this divisional application with the prior parent application, Serial No. 08/574,443, filed on December 15, 1995. The parent application was revived for purposes of continuity so that the present divisional application could be filed.

Several informalities in the specification have been corrected. These include changes on pages 9, 64, 81, 105, 109, 114, 123, 127, 134, 151, 159, 180 and 181, none of which is believed to have inserted new matter into Applicants' disclosure. Referring to the aforementioned page 81 (line 7), Applicants have corrected the description of an incompatible cell to mean "a cell *incapable* of processing RNA by removal of the processing element." The definition of an incompatible cell is in contrast to the definition of a compatible cell that precedes it. In the preceding lines on page 81, a compatible cell is defined as "a cell capable of processing RNA by removal of the processing element." See page 81, lines 5-6. In clarifying the definition of an incompatible cell, Applicants have corrected an obvious error in the specification that is clear from its context. Thus, no new matter has been inserted thereby. The issue of a "compatible cell" and "substantially removed" is discussed further below in the section dealing with the indefiniteness rejection under 35 U.S.C. §112, second paragraph.

For the sake of clarity and definiteness, relatively minor changes to claims 246, 247 and 251 have been effected above. All of these minor changes affect only the Markush language in the foregoing claims. It is believed that the amended claim language in these claims conforms to the

accepted proper useage under U.S. patent practice.

Entry of the above amendments to the specification and claims is respectfully requested.

Objection to Patent Drawings

Acknowledgement is made of the Notice of Draftperson's Patent Drawings Review that was issued in connection with this application. Formal drawings will be submitted as soon as allowable subject matter has been indicated in this application.

Submission of Sequence Listing

Applicants are filing concurrently with this Amendment a response to the Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

The Rejection for Double Patenting Under 35 U.S.C. §101

Claims 2-24 stand provisionally rejected under 35 U.S.C. §101 as claiming the same invention as that of claims 2-24 of copending Application Nos.: 08/978,632, 08/978,633, 08/978,634, 08/978,636, 08/978,637, 08/978,638, 08/978,639, and 08/574,443. As indicated by the Examiner on page 2 of the February 16, 1999 Office Action, "This is a provisional double patenting rejection since the conflicting claims have not in fact been patented."

As indicated above, claims 2-24 have now been canceled as they should have been when claims 245-302 were presented in Applicants' November 25, 1997 Preliminary Amendment. Any inconvenience caused by this oversight is sincerely regretted.

In view of the cancelation of claims 2-24, Applicants respectfully request withdrawal of the double patenting rejection

The Obviousness-Type Double Patenting Rejection

Claims 245-247 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 255, 257 [and] 259 of copending Application No. 08/978,636. In the Office Action (page 3), the Examiner stated:

> Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to the nucleic acid construct "which when introduced into a cell produces a nucleic acid product..." and claims 245-247 of '635 are drawn to "a process for... expressing a nucleic acid product in a cell....." The method is an obvious use of the claimed construct.
>
> This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The rejection for obviousness-type double patenting is respectfully traversed.

In response, Applicants and the present Assignee point out that it is their intention to maintain a line of demarcation between the subject matter of this application and that of their copending Serial No. 08/978,636. Because both applications are being presently prosecuted and it is uncertain at this point in time what will be the subject matter and language in any claims to be issued therefrom, Applicants respectfully request that the rejection for obviousness-type double patenting be held in abeyance until such time as subject matter is deemed allowable in either or both applications.

The Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 2-21 and 245 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the Office Action (page 4), the Examiner stated:

> Claims 2-21 are indefinite because they depend from canceled claim 1. Therefore claims 2-21 do not depend on any independent claim.
>
> Claim 245 is drawn to a method comprising a processing element "which when in a compatible cell... is substantially removed." This language is indefinite for failing to clearly define the meaning of "compatible cell" and the scope of the amount "substantially removed." Furthermore, it is not clear what the antecedent basis of "said process" in the preamble of the claim is, the "process for selectively expressing" or the processing function required for the product.

As indicated above, claims 2-24 have now been canceled as they should have been when claims 245-302 were presented in Applicants' November 25, 1997 Preliminary Amendment. Any inconvenience caused by this oversight is sincerely regretted.

With respect to claim 245, it is believed that the language in this claim passes muster under the statutory strictures for definiteness. Claim 245 recites "[a] process for selectively expressing a nucleic acid product in a cell, which product requires processing for functioning, the process comprising" two steps. The first step (i) calls for "providing a nucleic acid construct which when introduced into a cell produces a nucleic acid product comprising a non-native processing element, which when in a compatible cell, said processing element is substantially removed during processing." The second step (ii) in claim 245 calls for "introducing said construct into said cell."

It is believed that the terms "compatible cell" and "substantially removed" are well-defined in Applicants' disclosure. On page 81, first paragraph in the specification, Applicants disclose:

> The present invention provides (1) a universal composition for conditional nucleic acid processing by the introduction of a processing element into a nucleic acid sequence produced from a construct introduced into a cell. Said produced nucleic acid is processed in a ***compatible cell, i.e., a cell capable of processing RNA by removal of the processing element***. ***Said RNA is not processed in an incompatible cell, i.e., a cell incapable of processing RNA by removal of the processing element*** . . . [emphasis added]

Later, in the first paragraph on page 83, Applicants explain:

> Another significant aspect of this invention concerns a nucleic acid construct which when introduced into a cell produces ***a nucleic acid product comprising a non-native processing element which when in a compatible cell, the processing element is substantially removed during processing***. The processing element can comprise an RNA processing element including but not limited to an intron, a polyadenylation signal and a capping element, or combinations of the foregoing. [emphasis added]

In the last paragraph on page 83, Applicants reiterate the concept of a compatible cell when they describe:

> . . . a process for selectively expressing a nucleic acid product in a cell, the product being such that further processing is required for its functioning. The process comprises as its first step ***providing a nucleic acid construct which when introduced into a cell produces a nucleic acid product comprising a non-native processing element, which when in a compatible cell, the processing element being substantially removed during processing*** . . . [emphasis added]

It is believed that a reader skilled in the art would understand the meaning of the language in claim 245 regarding a "compatible cell" and "substantially removed," particularly taken with a reading of the specification. To be definite, the words and language in a claim need only reasonably apprise those skilled in the art as to the metes and bounds of the claimed invention. Clearly, the metes and bounds of the subject matter is sufficiently clear to meet the statutory test for definiteness.

In light of the cancelation of claims 2-24 and the foregoing remarks, it is respectfully requested that the rejection under 35 U.S.C. §112, second paragraph, be reconsidered and withdrawn.

The Rejection Under 35 U.S.C. §112, First Paragraph

Claims 2-21 and 245-251 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In the Office Action (pages 4-5), the Examiner stated:

> The constructs taught in the claims 2-24 are broadly drawn to a multitude of possible nucleic acid based constructs for use in a cell to produce a product (and in any context, *in vivo* or *in vitro),* comprising: (1) the construct as linear or circular, (2) the construct as comprising 1,2 or 3 strands, (3) comprising a terminus, a polynucleotide tail which can hybridize, (4) composed of RNA or DNA or combinations, (5)containing chemically modified nucleotides or analogs, (6) containing non-nucleic acid entities composed of polymers or ligands or a combination, (7) further specifying the natural and synthetic polymers, the synthetic homo- or heteropolymer with a net charge, (8)the construct imparting a "further biological activity" by the modified nucleotide, analog, entity, ligand or combination of those, further defined as nuclease resistance, cell recognition, cell binding, and cellular or nuclear localization or a combination, (9) a ligand attached to one of the modified nucleotides, etc. of claim 1, further described as attached to a "segment" or "tail" of the construct, and further defined as being a macromolecule or small molecule or combination. Claims 22-24 describe a second construct "which when present in a cell produces a product, said construct being bound non-ionically to an entity comprising a chemical modification or a ligand."
>
> Claims 245-254 are drawn to another broad genus of nucleic acid constructs for co-expression of a non-native polymerase and another nucleic acid sequence from the construct in a cell, again in any context, *in vivo* or *in vitro.* Dependent claims include the limitations: (1) a recognition site for the polymerase, (2) where the recognition site is complementary to a primer for the polymerase, (3) where the primer is tRNA, (4) where the polymerase is DNA polymerase, RNA polymerase, reverse transcriptase, or a combination, (5) where the RNA polymerase is a bacteriophage RNA polymerase, either T3, T7, SP6 or a combination, (6) a promoter for the RNA polymerase, (7) the nucleic acid produced is DNA, RNA, or a hybrid, chimera, or a combination and is sense or antisense DNA or RNA.

The Examiner went on to state further on pages 6-7:

> Claims 255-260 are drawn to another broadly claimed nucleic acid based construct for producing a non-native processing element

product in a cell which is substantially removed during processing (again, the claims could be read in any context, *in vivo* or *in vitro*).. The limitations further include: (I)an RNA processing element, selected from an intron, a polyadenylation and a capping element, or a combination, (2) a single stranded nucleic acid product, (3) a nucleic acid product selected from antisense RNA, antisense DNA, sense RNA, sense DNA, a ribozyme and a protein binding nucleic acid sequence or a combination, (4) and wherein said protein binding nucleic acid sequence comprises a decoy that binds a protein required for viral assembly or replication.

The specification teaches several constructs designed for entry into a cell and expression of one or more sequences to perform a biological function such as antisense inhibition of a nucleic acid. Specifically, several CHENAC constructs are taught prophetically, and pictured in figures 1-13 as vector based constructs constructed by using modified nucleic acid regions and designed to provide improved entry into a cell by way of improved construct-cell interaction. A second group of nucleic acid fused with antibody based constructs are taught prophetically and shown in figures 14-21. Preparation of multimeric insulin by means of nucleic acid hybridization is further taught prophetically and shown in figures 22-23. No exemplification for such constructs is taught in the specification as filed.

Furthermore, vectors ultimately designed for antisense inhibition of HIV in cells by co-expression of antisense DNA under control of a T7 promoter with a T7 polymerase (represented in figures 24-49) are taught and supported by *in vitro* data. Specifically, construction of the M13 phage vectors pRT-A, pRT-B, and pRT-c are taught which contain the coding sequence for the T7 RNA polymerase driven by the RSV promoter and with an SV40 intron sequence that will be spliced out to form a functional polymerase enzyme and each respective construct also having the

antisense A, B, and C sequences driven by a T7 promoter and terminated by a T7 terminator. A modified version of the pINT-3 construct (the parent vector of pRT-A, B and C vectors before insertion of the antisense sequences) is taught where a polylinker is inserted behind the poly-A tail of the T7 polymerase gene for subsequent sub-cloning of the lacZ gene in this instance to form pINT-LacZ. The result upon introduction in a eukaryotic cell would be synthesis of the T7 polymerase from the RSV promoter which in turn acts upon the T7 promoter to synthesize B-galactosidase.

Furthermore, plasmids are taught containing anti-sense segments introduced into the transcript region of the U1 gene, plasmid pHSD-4 U1 so that upon expression of the transcript, the antisense RNA sequence is produced to the complementary region of the HI genome. Specifically, pDU1-A, B, C and D were made using the antisense A, B, and C sequences previously described and D as a control containing a non-HIV sequence. A multi-cassette version of the constructs was also made by sub-cloning in tandem the A,B, and C antisense to make pNDU1 (A,B,C) (N meaning the construct was also contained the gene for neomycin resistance).

Further comments are provided on pages 8-10 in the Office Action where the Examiner stated:

> Other multi-cassette constructs taught were:
>
> (1) TRI 101, an M13 phage vector containing the "A" antisense T7 operon, the "B" antisense T7 operon and the "C" antisense T7 operon in a single construct (figure 46). Co-transfection would be required for expression of the antisense molecules from this construct with a vector that expresses T7 RNA polymerase (suggested is the intron containing construct of example 19); and,
>
> (2) an M13 construct constructed from a multi-ligation of portions of pINT-3 (containing the intron containing polymerase) and the T7 promoter driven A, B, and C sequences (see figure 47).
>
> The specification teaches application of some of these constructs ("various U1 constructs described above" p. 167, last line) in antisense inhibition of HIV in infected U937 cell culture. Specifically the following is shown: (1) expression of A, B, and C antisense by hybridization analysis after expression of the "U1 clone" (p. 169, line 3), (2) expression of the "triple U1 construct" (p. 169, para. (c), line 1) which result in a decrease in p24 production next to the control, and increased % reduction in p24 over time and after re-infection of cells, and these results were confirmed by absence p24 amplification next to control cells via PCR of the targeted DNA, and (3) expression of the construct of figure 50, a fusion product antisense A upstream of B-gal gene where antisense activity of the A portion caused inhibition of B-gal activity as shown in lacZ assays. The results in figure 51 show HIV A/Anti-A activity and HIV A/Anti-ABC (when the triple U1 construct was used by *co-transfection)* as the equivalent of the uninfected cells whereas the infected and control containing cells showed high B-gal expression. Therefore, it does not appear in the specification as filed that the multicassette A,B,C and T7 polymerase construct (expressed on same plasmid) was applied to the same HIV challenge experiments.
>
> Additional constructs are more prophetically taught: the primary nucleic acid construct that propagates production centers for the production of single-stranded antisense, etc. in examples 21-25, and the retrovirus vector containing sequences for the expression of antisense RNA directed at HIV on page 181, last para.
>
> Claims 22-24 read on any construct bound non-ionically to a ligand or otherwise chemically modified entity, further limited as having a polynucleotide tail terminus and where the tail is hybridized to a complementary polynucleotide sequence. The breadth of genus sought for such is not enabled in view of the lack of specificity of guidance in the specification as filed. The specification fails to provide guidance for the breadth claimed since the claims vaguely claim "constructs" which "produce products." The specification teaches only by way of example HIV inhibition by antisense expression from vector constructs which do not entail chemical modified entities nor polynucleotide termini.
>
> Claims 245-251 are further broadly drawn to the process of expressing a nucleic acid product in a cell which includes a

"processing element" that is "substantially removed during processing" in a "compatible cell." The language "processing element" reads on expression of any gene from said construct that has a "processing" function in a cell, for example, any ribozyme, polymerase, or any protein causing a modification of any molecule (protein or DNA)in a cell. The scope of the genus sought for the process of expressing such constructs is not enabled in view of the lack of specificity of guidance in the specification as filed. The specification falls to provide guidance for the breadth claimed since the claims nebulously claim "constructs' which produce "products" having a "processing" function. The specification teaches only prophetically an intron containing polymerase wherein the intron is removed in a compatible cell. The specification does not exemplify application of the T7 polymerase/U1-A,B,C vector as described in example 19 in cells It appears that only the U1A,B,C clone co-expressed with T7 polymerase (on another vector) is exemplified in the HIV challenge and LacZ assays.

The final comments of the Examiner on the enablement rejection are set forth on pages 10-12:

Furthermore, the claims specify the context for producing the product in any cell and no exemplification of whole organism success is found in the specification as filed. There is a high level of unpredictability in the antisense art and analogous gene therapy art for *in vivo* (whole organism) applications. The factors considered barriers to successful delivery of antisense delivery to the organism are: (1) penetration of the plasma membrane of the target cells to reach the target site in the cytoplasm or nucleus, (2) withstanding enzymatic degradation, and (3) the ability to find and bind the target site and simultaneously avoid non-specific binding (see Branch). Despite the synthesis of more resilient, nuclease resistant, oligonucleotide backbones and isolated successes with antisense therapy *in vivo,* the majority of designed antisense molecules still face the challenge of successful entry and localization to the intended target and further such that antisense and other effects can routinely be obtained. Note Flanagan et al. who teach "although numerous reports have cited antisense effects using oligonucleotides added to cell medium, direct proof that oligonucleotides enter cells and affect gene inhibition by an antisense mechanism is still lacking (page48, column 1)."

Specifically, *in vitro* results with one antisense molecule are not predictive of *in vivo* (whole organism) success. *In vitro,* antisense specificity to its target may be manipulated by "raising the temperature or changing the ionic strength, manipulations that are commonly used to reduce background binding in nucleic acid hybridization experiments." (Branch, p. 48) Discovery of antisense molecules with "enhanced specificity" *in vivo* requires further experimentation for which no guidance is taught in the specification. Note Branch who teaches the state of the art for designing an antisense which inhibits a target *in vivo:* it "is very difficult to predict what portions of an RNA molecule will be accessible *in vivo,* effective

antisense molecules must be found empirically by screening a large number of candidates for their ability to act inside cells (Branch, p.49)." And in the instant case, the claims read broadly on administration of an antisense inhibitor in any cell, therefore the whole organism included. While the specification teaches cell culture inhibition, no evidence of successful *in vivo* (whole organism) antisense inhibition has been shown, nor do the culture examples correlate with whole organism delivery.

One of skill in the art would not accept on its face the successful delivery of the disclosed antisense molecules *in vivo* in view of the lack of guidance in the specification and the unpredictability in the art. Specifically the specification does not teach (1) stability of the antisense molecule *in vivo,* (2)effective delivery to the whole organism and specificity to the target tissues, (3) dosage and toxicity, nor (4) entry of molecule into cell and effective action therein marked by visualization of the desired treatment effects. These key factors are those found to be highly unpredictable in the art as discussed *supra.* The lack of teaching of these factors in inhibition of the target, coupled to the amount of "trial and error" experimentation involved in the deduction of these results would lead one skilled in the art to necessarily practice an undue amount of experimentation *in vivo.*

No determination of enablement can be made for claims 2-21 because there is no independent claim from which they depend. Without knowing what claims 2-21 depend on, the full scope of the claims is not known.

The enablement rejection is respectfully traversed.

With respect to the application of the enablement rejection to claims 2-24, such grounds have been rendered moot, of course, by the cancelation of these claims.

With respect to claims 245-251, it is respectfully submitted that the subject matter of these claims is fully enabling such that a person skilled in the art could practice, without undue experimentation, Applicants' claimed invention.

As acknowledged in the Office Action, the specification teaches several constructs designed for entry into a cell and expression of one or more sequences to perfom a biological function such as antisense inhibition of a nucleic acid. Among these are several CHENAC constructs (see Figures 1-13), antibody based constructs (Figures 14-21) and multimeric insulin (Figures 22-23). Other embodiments include vectors designed for antisense inhibition of HIV in cells by coexpression of antisense DNA under control of a T7 promoter with a T7 polymerase (Figures 24-49) and plasmids containing antisense segments introduced

into the transcript region of the U1 gene. Also taught in Applicants' disclosure are other multi-cassette constructs, such as TRI 101 (an M13 phage containing the "A" antisense T7 operon, the "B" antisense T7 operon and the "C" antisense T7 operon in a single construct (Figure 46), and an M13 construct constructed from multi-ligation of portions of pINT-3 and the T7 promoter driven A, B and C sequences.

As also acknowledged in the Office Action, Applicants have provided examples that show antisense inhibition of HIV in infected U937 cell culture using various U1 constructs, expression of A, B and C antisense by hybridization analysis after expression of the U1 clone, and expression of the fusion product antisense A upstream of β-gal gene where antisense activity of the A portion caused inhibition of β-gal activity in lacZ assays (Figure 51). The assertion has been made that it does not appear in the specification as filed that the multicassette A, B, C and T7 polymerase construct was applied to the same HIV challenge experiments. In response, it should not be overlooked that under the law specific examples need not be given in the specification in order to satisfy the statutory requirements for enablement. All that is required is that the disclosure be enabling, that is to say, so that a person skilled in the art can practice the claimed invention, without undue experimentation. The fact that the same experiments for the U1 constructs were not specifically applied to the multicassette A, B, C and T7 polymerase constructs does not render the latter nonenabling. Again, the operative words under the enablement statute are "undue experimentation." Armed with Applicants' original disclosure, it is submitted that the skilled artisan could have practiced the presently claimied invention without undue experimentation.

Reconsideration and withdrawal of the enablement rejection are respectfully requested.

The First Rejection Under 35 U.S.C. §102

Claims 245-251 stand rejected under 35 U.S.C. §102(e) as being anticipated by Sullenger et al., U.S. Patent No. 5,854,038, issued on December 29, 1998, based upon an application filed on January 22, 1993. In the Office Action (pages 12-13), the Examiner stated:

> The claimed invention is drawn to a process of using a nucleic acid construct which when introduced into a cell produces a nucleic acid product comprising a non-native processing element, which when in a compatible cell, said processing element is substantially removed during processing. Further limitations include an RNA processing element (an intron or a polyadenylation signal and capping element), the nucleic acid product being: single stranded, antisense DNA or RNA, sense DNA or RNA, a ribozyme or a protein binding sequence such as one that binds protein required for viral assembly or replication, and introduction of the construct in to a cell or whole organism.
>
> Sullenger et al. teach a method of expression of RNA-based inhibitors of viral replication by localization of an inhibitory RNA such as a ribozyme to a cellular target. Ribozymes are known in the art to have a processing function and are also have an inherent half-life and are therefore removed.

The anticipation rejection by Sullenger et al. is respectfully traversed.

Applicants respectfully contend that there is a lack of identity of material elements between their instantly claimed invention and Sullenger's disclosure.

Reconsideration and withdrawal of the anticipation rejection are respectfully requested.

The Second Rejection Under 35 U.S.C. §102

Claims 22-24 stand rejected under 35 U.S.C. §102(e) as being anticipated by Meyer et al., U.S. Patent No. 5,574,142, issued on November 12, 1996. In the Office Action (page 13), the Examiner stated:

> The claimed invention is drawn to any construct which when present in a cell produces a product, and is bound non-ionically to an entity comprising a modification or a ligand, and further comprises a hybridized polynucleotide tail.
>
> Meyer et al. teach a covalently linked conjugate of an oligonucleotide (ODN) with a peptide and a carrier or targeting ligand (ODN-peptide-carrier) including a therapeutic oligonucleotide which is capable of selectively binding to a target sequence of DNA, RNA or protein inside a target cell. The invention of Meyer et al. Reads on all of the instant claimed limitations for a non-naturally occurring

construct for production of a product in a cell (in Meyer, an antisense oligonucleotide is produced).

In view of the cancelation of claims 2-24 above, it is believed that the anticipation rejection by Meyer et al. has been rendered moot and irrelevant. Reconsideration and withdrawal of this rejection are respectfully requested.

The Third Rejection Under 35 U.S.C. §102

Claims 245-251 stand rejected under 35 U.S.C. §102(e) as being anticipated by Hurwitz et al., U.S. Patent No. 5,648,243, based upon an application filed on July 31, 1991. In the Office Action (page 14), the Examiner stated:

> The claimed invention is drawn to a nucleic acid construct which when introduced into a cell produces a nucleic acid product comprising a non-native processing element, which when in a compatible cell, said processing element is substantially removed during processing. Further limitations include an RNA processing element (an intron or a polyadenylation signal and capping element), and the nucleic acid product being: single stranded, antisense DNA or RNA, sense DNA or RNA, a ribozyme or a protein binding sequence such as one that binds protein required for viral assembly or replication.
>
> Hurwitz et al. teach selective use of introns in an expressed gene for increased expression of the gene in a mammalian cell, specifically the product is human serum albumin.

The anticipation rejection by Hurwitz et al. is respectfully traversed.

It is respectfully contended that Hurwitz' patent neither discloses nor suggests Applicants' claimed invention. Reconsideration and withdrawal of this anticipation rejection is respectfully requested.

The Fourth Rejection Under 35 U.S.C. §102

Claims 245-251 stand rejected under 35 U.S.C. §102(b) as being anticipated by De Young et al. ["Functional Characterization of Ribozymes Expressed Using U1 and T7 Vectors for the Intracellular Cleavage of ANF mRNA," Biochemistry

33:12127-12138 (1994)]. In the Office Action (pages 14-15), the Examiner stated:

> The claimed invention is drawn to a nucleic acid construct which when introduced into a cell produces a nucleic acid product comprising a non-native processing element, which when in a compatible cell, said processing element is substantially removed during processing. Further limitations include an RNA processing element (an intron or a polyadenylation signal and capping element), and the nucleic acid product being: single stranded, antisense DNA or RNA, sense DNA or RNA, a ribozyme or a protein binding sequence such as one that binds protein required for -viral assembly or replication.
>
> De Young et al. teach expression of ribozymes imbedded in a U1 sequence and under the control of a T7 promoter. Ribozymes are known in the art to have a processing function and also have an inherent half-life and are therefore removed.

The anticipation rejection by De Young et al. is respectfully traversed.

It is believed that De Young's disclosure does not anticipate the present invention.

Reconsideration and withdrawal of the fourth anticipation rejection are respectfully requested.

* * * * * * *

SUMMARY AND CONCLUSIONS

Claims 245-251 are being presented for further examination, with claims 2-24 having been canceled and claims 246, 247 and 251 having been amended above.

This Amendment is being accompanied by a Request For An Extension Of Time (3 months) and authorization for the small entity fee therefor. No other fee or fees are believed due for filing this Amendment. In the event that any other fee or fees are due, however, authorization is hereby given to charge the amount of any such other fee(s) to Deposit Account No. 05-1135, or to credit any overpayment thereto.

If a telephone conversation would further the prosecution of the present application, Applicants' undersigned attorney request that he be contacted at the number provided below.

Respectfully submitted,

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